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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/527,831	01/09/2006	Kathryn Nance North	2202530.125/GTI-013	1014

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EXAMINER
POHNERT, STEVEN C

ART UNIT	PAPER NUMBER
1634	

NOTIFICATION DATE	DELIVERY MODE
11/28/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/527,831	NORTH, KATHRYN NANCE	
	Examiner	Art Unit	
	Steven C. Pohnert	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 August 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,5,10,12-16,18,24,25,29,33,34 and 41-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,5,10,12-16,18,24,25,29,33,34 and 41-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 March 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/13/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This action is in response to papers filed 8/13/2008.

The written description rejection of claims 1, 4-5, 10, 12-16, 18, 24-25, 29, 33-34 has been withdrawn in view of the amendment.

The scope of enablement rejection of 1, 4-5, 10, 12-16, 18, 24-25, 29, 33-34 has been withdrawn in view of the amendment of the claims to predict potential sprinting, strength or power performance is positively associated with the presence of a 577R allele in a human subject in view of the arguments and the art of Drzhevskaya and Delmonico. The art of record thus suggest that the presence of the 577R allele does indicate improved potential for strength, power, or sprint performance.

Claims 1, 4-5, 10, 12-16, 18, 24-25, 29, 33-34 and 41-44 are pending.

This action is FINAL.

Claim Rejections - 35 USC § 101-New Grounds

1. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1, 4-5, 10, 12-16, 18, 24-25, 29, 33-34 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The claims 1, 4-5, 10, 12-16, 18, 24-25, 29, 33-34, are drawn to methods of predicting athletic performance in a human by determining whether a human has at least one copy of the 577R allele at the locus encoding the alpha-actinin 3 gene, wherein the presence of at least one allele predicts positive potential in sprinting, strength or power. The methods as claimed, do not meet the machine or physical

transformation required by the CAFC court as described in *In re Bilski*. The claims as written encompass mere mental steps i.e. determining a genotype for future use and predicting potential, sprinting, strength or power performance. The step of determining the presence of a 577R allele does not require the use of a machine or result in a physical transformation. Determining could be directed merely to looking at a database file on a computer or a patient chart.

The claims 41-44 are drawn to methods of predicting athletic performance in a human by determining whether a human has the genotype 577XX at the locus encoding the alpha-actinin 3 gene, wherein the presence 577XX genotype predicts a negative potential in sprinting, strength or power. The methods as claimed, do not meet the machine or physical transformation required by the CAFC court as described in *In re Bilski*. The claims as written encompass mere mental steps i.e. determining a genotype for future use and predicting potential, sprinting, strength or power performance. The step of determining the presence of a 577XX allele does not require the use of a machine or result in a physical transformation. Determining could be directed merely to looking at a database file on a computer or a patient chart.

These rejections can be easily be overcome by amending the step to require obtaining a sample from a human and genotyping the sample.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 41-44 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of determining sprint, strength, or power performance in human males comprising: obtaining a sample from a male, analyzing the sample for the presence of the human ACTN3 577R allele, wherein the presence of the presence of ACTN3 577R allele indicates an negative correlation of sprint, strength or power performance in humans does not reasonably provide enablement for predicting a negative correlation with sprint performance, endurance performance, power performance, or strength performance in any subject by the presence of the 577XXgenotype. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. These factors have been described by the court in re Wands, 8 USPQ2d 1400 (CA FC 1988). Wands states at page 1404,

"Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in the Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence of working examples, (4) the nature of the

invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention and the breadth of the claims:

The claims encompass predicting athletic performance in "any" any human based on the presence of the 577XX genotype of ACTN3, wherein the presence of the ACTN3 577XX genotype is negatively correlated with potential sprinting, strength or power performance of the human.

The amount of direction or guidance and the Presence and absence of working examples.

The specification teaches a study of Caucasian controls and elite athletes comprising 108 endurance and 83 endurance athletes, 88 African Zulu and 152 Australian Caucasian individuals, that elite sprint athletes had a lower frequency of the 577XX genotype of ACTN3 (6% versus 18% in Caucasian population, $p<0.05$)(see paragraph 100 and 102). Thus the specification teaches that elite sprint athletes were less likely to have the 577XX allele than the controls. Thus the specification teaches trained elite sprint athletes are more likely to have the 577RR genotype than untrained. It is noted that the elite sprint group is a group that has been selected by performance and thus may not be representative of the population as a whole.

The specification further teaches in 46 track athletes competing in events of 800m, 42 swimmers competing in events of 200 m, 9 judo athletes, 7 short-distance track cyclists, and 3 speed skaters. For comparison, a subset of 194 subjects (122 male and 72 female) classified independently as specialist endurance athletes and analyzed,

including 77 long-distance cyclists, 77 rowers, 18 swimmers competing over distances of 400 m, 15 track athletes competing in events of 5,000 m, and 7 cross-country skiers. Thirty-two sprint athletes (25 male and 7 female) and 18 endurance athletes (12 male and 6 female) had competed at the Olympic level (paragraph 0103). The specification further teaches "genotypic profiles of the three control groups (150 blood donors, 71 healthy children, and 215 healthy adults) did not differ significantly from one another (x^2=0.19; P=0.996) nor from a previously genotyped group of 107 white Europeans" (paragraph 104).

The specification further teaches there was no significant genotype difference between the elite athletes and control (paragraph 105), although a strong association was seen in sprint athletes relative to controls ($x^2_{[df=5]}$=23; P<0.001) (see paragraph 105). The significant allele frequency differences were seen between sprint athletes and controls for both males ($x^2_{[df=1]}$=14.8; P<0.001) and females ($x^2_{[df=1]}$=7.2; P<0.01) (see paragraph 105). Further the specification teaches that the allele frequencies deviated significantly in opposite directions in the sprint and endurance athletes (both males ($x^2_{[df=1]}$=13.3; P<0.001) and females ($x^2_{[df=1]}$=5.8; P<0.05) (see paragraph 105). The specification teaches there were allelic difference between the trained elite athletes and controls. However, as the trained elite athletes have undergone a selection process based on performance and training it is unpredictable that the correlation are the only factor in athletic performance.

In example 3 the specification teaches that there is a trend toward significance of the 577XX genotype in endurance athletes, although this reaches statistical significance

only in females (see paragraph 110). The specification thus teaches the 577XX genotype of ACTN3 is associated with increased endurance potential in females, but there is a trend toward this in males. The specification thus does not teach or suggest that the 577XX genotype is negatively associated with sprinting, strength or power, but merely suggests it may be associated with improved endurance performance. Improved endurance performance is not predictably associated with negative sprint, power, or strength performance.

In summary the specification teaches that there is no significant difference between elite athletes and controls, although there was a difference in sprint athletes, both male and female. Further the specification teaches there was a significant allele frequency difference between elite endurance athletes and elite sprint athletes.

The state of prior art and the predictability or unpredictability of the art:

The prior art teaches the ACTN3 577X mutation has arisen in humans following the evolution of the ACTN3 gene from primates (Mills et al (Human Molecular Genetics (2001) Volume 10, pages 1335-1346) (see abstract). Mills teaches that ACTN3 is a homolog of ACTN2 (see abstract). Mills teaches there are four different ACTN homologs in mice and humans. Mills further teaches that the mouse ACTN3 may not be functionally redundant with the human ACTN3 (see page 1340, 2nd column, 1st full paragraph). Mills teaches that unlike humans and primates, ACTN2 is expressed in many fibers that do not express ACTN3, thus suggesting different regulation and/or function in mouse muscle fibers (see page 1339, 1st column). Mills further teaches ACTN3 homologs have not been isolated in other mammals (see page 1340, 2nd

column, last paragraph). Mills teaches the ACTN3 577X allele has resulted due to a single mutation after the divergence of humans and chimpanzees from other mammals (see page 1340, 1st column, last 3 lines). Mills thus teaches that neither the 577X allele nor the ACTN3 gene is predictably found in "any" mammal.

Gene card (genecards.org/cgi-bin/carddisp.pl?gene=ACTN3&search=actn3&suff=txt, pages 1-11, 3/24/2007) teaches ACTN3 homologs have only been found in dog, fruitfly, zebrafish, mouse, chimpanzee, and rat (see page 11), while listing 32 species in which a homolog of ACTN3 has not been found. Genecard teaches there are 16,406 bases in the ACTN3 gene. Genecard further teaches there are 9 known SNPs in the human ACTN3 gene and 33 cDNAs. Genecard thus teaches ACTN3 is not predictably present in all species.

Post filing art teaches that the frequencies of the R577X alleles in elite distance runners from Ethiopia and Kenya did not significantly differ from those of their respective control population (see Yang, et al (Med. Sci. Sport and Exercise (2005) volume 37, s42). Yang et al further teaches, "this polymorphism does not contribute significantly to the phenomenal success of elite East African endurance runners."

Moran et al (European Journal of Human Genetics (2007) volume 15, pages 88-93) teaches in a study of 992 adolescent Greeks the presence of the 577R allele resulted in a significant association with sprint times over 40m in males, but not females (see abstract and table 1). However, Moran did not find any other significant correlation of the 577R with tests of power including handgrip strength, basketball throw, vertical jump or agility run (see table 1). Moran further tested aerobic capacity or VO2 max

(commonly used tests of endurance performance) and did not see a significant relationship with the 577X allele (see table 1). Moran et al further teaches, "We found no evidence that the R577X genotype is associated with endurance or obesity related genotypes" (see page 93, 1st column last paragraph). Moran thus teaches the 577R allele is only predictably associated with sprint speed in males. Moran further teaches that the 577R allele is not predictably associated with any other power testing performed. Moran further teaches that the 577X allele is not predictably associated with endurance performance.

Lucia et al studied the frequency of the ACTN3 genotype in a group of 50 top level professional cyclists and 52 Olympic class endurance runners (International Journal of Sports Medicine(2006) volume 27, pages 880-884). Lucia study demonstrated there was no significant differences between the elite runners and cyclists and the R577X genotype. Thus Lucia teaches it would be unpredictable to associate the R577X genotype with improved endurance performance.

Pitsiladis et al (Lancet (2005) volume 366, pages s16-s17) teaches, "Although ACTN3 is an interesting candidate gene of physical performance, the use of a genetic test for this one gene to assess potential for athletic success cannot be justified given the multifactorial nature of sporting performance. Others have been persuaded to consider multiple genes when examining multifactorial traits such as physical performance. A professional Australian Rugby team called the Sea-Eagles has, for example, admitted genotyping 18 of their 24 players for 11 exercise-related genes and tailoring exercise training for the individuals on the basis of their results. Although some

genes do affect the interindividual variation in physical performance and trainability, this knowledge cannot be used to predict sporting talent or to prepare a training schedule. The current genetic evidence does not warrant genotyping an individual to establish their ability to run fast when this trait can be measured far more effectively with a stopwatch." Thus Pitsiladis suggests genotyping to determine athletic performance is unpredictable.

The level of skill in the art:

The level of skill in the art is deemed to be high.

Quantity of experimentation necessary:

In order to practice the invention as claimed the artisan would first have to determine if the presence of the 577XX genotype is negatively associated with potential sprinting, strength or power performance. This would taken undue trial and error experimentation, as the instant specification nor the prior art teaches or suggests that such an association exists. Thus the artisan would have to first determine what is encompassed by a negative association with potential sprinting, strength or power performance. This would require undue trial and error experimentation as there is no guidance. The artisan would have to determine if this requires the inability to sprint, have strength or power performance, or just the inability to compete at an elite level in such events.

Once the artisan determine what is broadly encompassed by a negative association with potential of sprint, power or strength performance the artisan would then have to determine if the 577XX genotype of ACTN3 is indicative of such a negative

association. This would require undue trial and error experimentation as the specification nor art teach or suggest such a relationship, but merely suggests that the 577XX genotype is more often found in endurance athletes, which does not mean these athletes have a negative potential in sprinting, power or strength, but that they have a better aptitude toward endurance type events.

Therefore, in light of the breadth of the claims, the lack of guidance in the specification, the high level of unpredictability in the associated technology, the nature of the invention, the negative teachings in the art, and the quantity of unpredictable experimentation necessary to practice the claimed invention, it would require undue experimentation to practice the invention as claimed.

Response to arguments

The response on page 7, asserts that Table 1 demonstrates that the presence of 577XX genotypes is indicative of a negative correlation with sprint, power, or strength performance. This arguments has been thoroughly reviewed but is not considered persuasive as table 1 merely demonstrates that the 577XX genotype is under represented in males and females that are in sprint or power sports at an elite level and is more common in endurance athletes. This does not suggest that athletes with 577XX genotype have negative potential for sprinting, but merely suggest that athletes with the 577XX are more likely to be an endurance athlete.

Using the criteria of the instant specification and the approach used in crafting claim 41, Michael Phelps would be considered an elite endurance athlete due to his performance in the 400 individual medley, but is also an elite sprinter as one of the elite

100 meter freestylers and butterfliers in the world. Thus implying an athlete is elite as an endurance athlete does not predictably suggest the athlete has negative potential as a sprinter as the logic that is being used to suggest that claims 41-44 are supported by the specification.

4. Claims 41-44 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a new matter rejection.

Claim 41 and dependent claims 42-44 have been added by the instant amendment. Claim 41 is drawn to a method to predict potential athletic performance in a human comprising: a) determining whether the human has the genotype 577XX at the locus encoding amino acid number 577 of the human a-actinin-3 (ACTN3) protein; and b) predicting the potential sprinting, strength or power performance of the human, the presence of the 577XX genotype being negatively associated with potential sprinting, strength or power performance. Thus the claims are drawn to the presence of the 577XX genotype being negatively associated with strength, power or sprint performance. The response on page 7, asserts that Table 1 demonstrates that the presence of 577XX genotypes is indicative of a negative correlation with sprint, power, or strength performance. This arguments has been thoroughly reviewed but is not considered persuasive as table 1 merely demonstrates that the 577XX genotype is

under represented in males and females that are in sprint or power sports at an elite level and is more common in endurance athletes. This does not mean suggest that these athletes with 577XX genotype have negative potential for sprinting, but merely suggest that athletes studied with the 577XX have more likely to be an endurance athlete. The claim as written in view of the specification requires that an athlete that is good at an endurance event is a poor sprinter, which is not necessarily true as exemplified by Michael Phelps, who is an elite endurance athlete in the 400 individual medley, while also being an elite sprinter in the 100 freestyle and the 100 butterfly. Thus the mere teachings of the specification that the 577XX genotype is more common in endurance athletes than in sprinters does not provide support for the 577XX genotype being negatively associated with sprint, power or strength performance. Thus specification does not teach or suggest that the 577XX genotype is indicative of a negative association with sprint, power or strength performance.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1, 4-5, 10, 12-16, 18, 24-25, 29, 33-34 and 41-44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 4-5, 10, 12-16, 18, 24-25, 29, 33-34 are indefinite because it lacks a positive active step relating back to the preamble. The preamble recites a method of predicting potential athletic performance in a human, however the last positive active step is drawn to predicting positive potential of sprinting, strength, or power

performance. Therefore it is unclear as to whether the method is drawn to predicting athletic performance in a human or predicting positive potential of sprinting, strength, or power performance. This rejection can easily be overcome by amending the preamble to be drawn to a method of predicting potential sprint, strength or power performance

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Summary

No claims are allowed.

Conclusion

1. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Steven C. Pohnert whose telephone number is (571)272-3803. The examiner can normally be reached on Monday-Friday 6:30-4:00, every second Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Steven Pohnert

/Sarae Bausch/
Primary Examiner, Art Unit 1634